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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/086,206	02/28/2002	Juana Magdalena	408.014-CON	1829

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EXAMINER	
JOHANNSEN, DIANA B	
ART UNIT	**PAPER NUMBER**
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/086,206	MAGDALENA ET AL.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-32,34-44 and 47-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *31,32 and 34* is/are allowed.

6)☒ Claim(s) *28-30,35-44,47-51,54 and 55* is/are rejected.

7)☒ Claim(s) *41 and 47-53* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/242,588.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is responsive to the Amended Response including a complying complete set of claims filed January 9, 2007. Claims 31, 34-38, 41-43, 47, and 54-55 have been amended and claim 33 has been canceled. Claims 28-32, 34-44, and 47-55 are now pending and under consideration. Applicants' amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections and/or objections not reiterated in this action have been withdrawn. **This action is FINAL.**

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

3. Claims 52-53 remain objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim may refer to other claims in the alternative only. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

It is noted that the response of January 9, 2007 indicates that claim 52 has been amended so as to refer to other claims in the alternative. However, the claim has not in fact been so amended.

2. Claim 41 is objected to because of the following informalities: the claim contains a typographical error, reciting "dioxygenin" rather than "digoxigenin."

3. Claims 47-51 are objected to because of the following informalities: independent claim 47, at line 1, refers to a mycobacteria "stain" rather than a mycobacteria "strain."

Claim Rejections - 35 USC § 112, second paragraph

4. Claims 28-30, 35-40, 42-44, 47-51, and 54-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 28-30, 37-40, 42-44, 47-51, and 54-55 remain indefinite over the recitation of the term "specific" in the claims. It is unclear as to what is meant by the term "specific", and as to how this term is intended to limit the claims. For example, what structural and/or functional properties would be required of a nucleic acid in order for it to be considered "specific to members of the *M. tuberculosis* complex"? The response traverses the rejection on the grounds that it is "well known by the one skilled in the art that 'specific' means 'pertaining to a species,' 'produces by a single kind of microorganism' (see www.biology-online.org/dictionary/specific). 'characteristic of a defined biological species' (see www.granddictionnaire.com)." The response further argues that "this term in the claims does not limit the structural and/or functional properties of the nucleic acids which are also precisely defined by their sequence." These arguments have been thoroughly considered but are not persuasive. First, it is noted that the *M. tuberculosis* complex comprises multiple species (e.g., *M. bovis, M. microti, M. tuberculosis, M. africanum*, etc.). Thus, applicants' argument that the term "specific" refers to a single species or organism merely reinforces the examiner's argument that the term within the context of the claims is confusing. If "specific" refers to a single species or kind of microorganism, which member of the *M. tuberculosis* complex is referenced by this language? Further, the nucleic acids of the claims, while

referenced by SEQ ID Nos, are not "precisely defined by their sequence." For example, claims 28-30 recite the open transitional language "having"/"has" such that the claims may encompass molecules comprising additional sequences flanking the recited SEQ ID Nos. While the recitation "specific to mycobacteria of *M. tuberculosis* complex" appears to be an attempt to further limit the molecules of the claims to a subset of molecules comprising the recited SEQ ID Nos that have some additional functional characteristics, the extent to which the claims are limited is not clear because the term "specific" as used does not have a clear and definite meaning that would allow one of skill to recognize what is encompassed by the claims. Accordingly, this rejection is maintained.

Claims 42-44, 47-51, and 54-55 remain indefinite over the recitation of the limitations "the nucleotide sequence of sequences adjacent to the senX3-regX3 region in the 3' of senX3 region," and "the nucleotide sequence of sequences adjacent to the senX3-regX3 region in the 5' of regX3 region" in claims 42, 47, 54, and 55. There is insufficient antecedent basis for the limitations "the nucleotide sequence...", "the senX3-regX3 region...", "the 3' of senX3 region," and the 5' of regX3 region" in the claims, as the claims do not previously refer to these sequences/regions. The claims should be amended so as to provide a clear and limiting structural and/or functional description of those primers that are intended to be encompassed by the claims. It is noted that the response states that the claims have been amended to overcome the rejection; however, the amendments referenced in the response have not in fact been made. Accordingly, this rejection is maintained.

Claims 47-51 remain indefinite because the relationship between steps 2-3 of claim 47 are unclear. It is noted that step 3 refers both to contacting the probe with "the biological sample" and with "amplified sequences." It is not clear whether step 3 is to be performed using sequences amplified in step 2, or using the original "biological sample." Clarification is required. It is noted that the response indicates that the claim has been amended to clarify the relationship between steps 2 and 3; however, no such amendment has been made. Accordingly, this rejection is maintained.

Claim 55 remains indefinite over the recitation of the limitation "the specific nucleic acids" in step (1), because there is insufficient antecedent basis for this limitation in the claim. Although the response indicates that the claim has been amended to recite "the specific nucleotide sequence" in lieu of "the specific nucleic acids," this amendment was not made. This rejection is maintained.

Claims 55 remains indefinite because the relationship between steps 2-3 of claim 55 are unclear. It is noted that step 3 refers both to contacting the probe with "the biological sample" and with "amplified sequences." It is not clear whether step 3 is to be performed using sequences amplified in step 2, or using the original "biological sample." Clarification is required. It is noted that the response indicates that the claim has been amended to clarify the relationship between steps 2 and 3; however, no such amendment has been made. Accordingly, this rejection is maintained.

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANTS' AMENDMENTS:

Claim 35 is indefinite over the recitation of the limitation "the sequences comprising sequence SEQ ID No: 1 or the complement of SEQ ID No: 1 or their corresponding RNA sequences or their corresponding gene" because there is insufficient antecedent basis for this limitation in the claims.

Claim 36 is indefinite over the recitation of the limitation "the sequences comprising two successive sequences SEQ ID No: 1 followed by a sequence SEQ ID No: 2 or their corresponding RNA sequences or their corresponding gene" because there is insufficient antecedent basis for this limitation in the claims.

Claims 42-43 and 54 are indefinite over the recitation of the limitation "one primer consists of (claim 42)/consisting of (claim 54) the nucleotide sequence of sequences adjacent to the senX3-regX3 region in the 3' of senX3 region and other primer consists of (claim 42)/consisting of (claim 54) the nucleotide sequence of sequences adjacent to the senX3-regX3 region in the 5' of regX3 region" in claims 42 and 54. This limitation refers to single, particular sequences of which the claimed primers "consist." However, the claim does not make clear what these particular sequences are, and further, the specification never discloses any single, particular "nucleotide sequence of sequences adjacent to" the recited regions, as would be necessary for one of skill in the art to understand what sequences are actually encompassed by the claims. Thus, it is not clear what primers are actually encompassed by the claims. It is noted that dependent claim 44 is clear because it recites the actual sequences of the claimed molecules.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANTS' AMENDMENTS:

6. Claims 36, 42-44 and 54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Regarding claim 36, the claim has been amended such that it refers to a probe or primer that hybridizes with "one of the sequences comprising two successive sequences SEQ ID No: 1 followed by a sequence SEQ ID No: 2 or their corresponding RNA sequences or their corresponding gene." While the specification discloses a probe that actually comprises "two successive sequences SEQ ID No: 1 followed by a sequence SEQ ID No: 2," the claim as written encompasses any probe or primer that hybridizes to such a molecule, or to RNA sequences or genes that "correspond" to "two successive sequences SEQ ID No: 1 followed by a sequence SEQ ID No: 2." The specification as filed does not disclose this broad genus of molecules. It is also noted that applicant has not identified where in the originally filed specification basis for these amendments is believed to be found.

Regarding claims 42-44 and 54, claims 42-44 as amended include the recitation of the limitation "one primer consists of (claim 42)/consisting of (claim 54) the nucleotide

sequence of sequences adjacent to the senX3-regX3 region in the 3' of senX3 region and other primer consists of (claim 42)/consisting of (claim 54) the nucleotide sequence of sequences adjacent to the senX3-regX3 region in the 5' of regX3 region" in claims 42 and 54. This limitation refers to single, particular sequences of which the claimed primers "consist." However, the originally filed specification does not refer to any such single, particular molecule (for example, the specification never sets forth a particular sequence or region that corresponds to this language). Thus, the specification does not appear to provide basis for the particular sequences referenced in the claims as amended. It is also noted that applicant has not identified where in the originally filed specification basis for these amendments is believed to be found.

Claim Rejections - 35 USC § 102

7. In view of the cancellation of claim 33, the rejection of the claim under 35 U.S.C. 102(e) as being anticipated by Stover et al (U.S. Patent No. 5,700,683 [12/1997; filed 2/1995]) set forth in the Office action of February 10, 2006 is moot.

8. In view of the amendment of claim 37 such that the claim requires a probe that "consists of a region of sequence SEQ ID No: 2 comprising the GAG codon in positions 40 to 42 or the complement of said region," and in view of the amendment of claim 42 to require primers that "consist of" particular nucleotide sequences, the rejection of claims 37 and 42-43 under 35 U.S.C. 102(e) as being anticipated by Stover et al (U.S. Patent No. 5,700,683 [12/1997; filed 2/1995]) set forth in the Office action of February 10, 2006 is withdrawn.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANTS' AMENDMENTS:

10. Claims 35-36 and 41 are rejected under 35 U.S.C. 102(e) as being anticipated by Stover et al (U.S. Patent No. 5,700,683 [12/1997; filed 2/1995]).

Stover et al disclose primers and probes that may be used to differentiate BCG strains of *M. bovis* from *M. tuberculosis* and virulent *M. bovis* strains (see entire reference, particularly column 1, line 40-column 2, line 12, and column 11, line 40-column 14, line 63). Preferred molecules disclosed by Stover et al include those of Table 1 and the primers set forth in column 14 at lines 55-62.

With regard to claims 35-36 and 41, it is noted that the claims merely requires a probe or primer that "hybridizes at 68°C in a 5xSSC hybridization buffer" to one of the recited molecules (which include "corresponding" RNA molecules and genes). As 5xSSC constitutes a high salt, permissive hybridization solution, the primers taught by Stover et al (all of which also meet the length requirement of the claims) anticipate the claimed invention. With further regard to the recitation in claim 41 "which is labeled by dioxygenin [sic]," it is noted that the claim as written is not limited to probes/primers that include digoxigenin; rather, the claim may be interpreted as requiring primers/probes that hybridize to target sequences labeled with digoxigenin. As it is an inherent property of the primers taught by Stover et al that they would hybridize to the sequences of the claims regardless of whether the sequences include digoxigenin, the primers of Stover et al meet the requirements of claim 41.

11. Claim 37 is rejected under 35 U.S.C. 102(b) as being anticipated by Brennan (US 5,474,796 A [12/1995]).

The claim is drawn to a "nucleotide probe for detection of specific sequences of nucleic acids of M. tuberculosis complex other than BCG wherein said probe consists of a region of sequence SEQ ID No: 2 comprising the GAG codon in positions 40 to 42 or the complement of said region."

Brennan discloses an array of oligonucleotides comprising all possible 10-mers (see entire reference, particularly Example 4), and thus teaches probes that "consist of a region of sequence SEQ ID No: 2 comprising the GAG codon in positions 40 to 42 or the complement of said region." Further, it is noted that the instant claim is not drawn,

e.g., to a method in which any particular bacteria are detected; rather, the claim is drawn to a probe "for detection of specific sequences of nucleic acids of M. tuberculosis complex other than BCG." As the probes of Brennan could be used in the specific detection of any *M. tuberculosis* complex species (for example, by sequencing), the probes of Brennan meet the requirements of the claim. Thus, Brennan anticipates claim 37.

Claim Rejections - 35 USC § 103

12. In view of the amendment of claim 54 to require primers that "consist of" particular nucleotide sequences, the rejection the claim under 35 U.S.C. 103(a) as being unpatentable over Stover et al (U.S. Patent No. 5,700,683 [12/1997; filed 2/1995]) in view of Ahern (The Scientist 9(15):20 [7/1995]) is withdrawn.

Conclusion

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday and Thursday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571/272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Diana B. Johannsen
Primary Examiner
Art Unit 1634